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UNIVERSITY RESEARCH ADMINISTRATION  
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National Human Research Protection  
Advisory Committee (NHRPAC)  
Attn: Dr. Greg Koski  
6100 Executive Boulevard, Suite 3B01  
MSC-7507  
Rockville MD 20892-7507

Dear Dr. Koski:

The Office of Human Research Protection (OHRP) recently placed a document on its website with a request for comment. The document labeled "draft interim guidance," is entitled: "Financial Relationships in Clinical Research: Issues for Institutions, Clinical Investigators, and IRBs to Consider when Dealing with Issues of Financial Interests and Human Subjects Protection." (referred to hereafter as Guidance) This letters responds to the proposed Guidance on behalf of the University of Chicago.

The University of Chicago understands and agrees with OHRP that clinical investigators and their institutions must conduct their research programs involving human subjects with unquestionable moral principles and scientific integrity. Without public confidence in the manner in which clinical research is conducted in our academic biomedical programs, subjects will reluctant to become involved with trials and other research endeavors dependent on human volunteers. So, although we agree with the principles articulated by OHRP, we find serious flaws in the draft document. Our comment letter is based on discussions with senior clinical researchers and institutional officials and our biomedical IRB Chair and IRB members. The major issues of concern are described below.

Our IRB members question the factual basis for concluding that increased IRB oversight of ALL cases in which the institution has determined that the conflict of interest cannot be eliminated but can be managed will improve protections for human subjects. (reference section 4. 4.3 of Guidance) This expectation is excessively burdensome on the IRB and may not improve the protections for human subjects. For many IRB members, the relevance of loading the Informed Consent with disclosures of *de minimus* consulting or speaking arrangements with clinical sponsors for any one of the involved clinical investigators is seriously in question. Various IRB members noted the chilling effect these additional responsibilities could place recruitment and retention of a senior experienced IRB members. They are concerned further that OHRP's expectations for reassessment of all managed conflicts would cut in half the time the IRB has to judge more substantive ethical and research protections. They fear this oversight would have a chilling effect on innovation in clinical research, critical relationships with small

businesses and, in fact, place more authority in the persuasive weight of large pharmaceutical relationships.

We urge that OHRP reconsider the Guidance document. We believe that thresholds should be established for those disclosed conflicts where the institution has an approved management plan. This would minimize repetitious IRB of disclosed and institutionally-managed investigator conflicts of interest and focus the IRB's efforts where serious re-consideration may be merited. We agree that the IRB and institutional committees and officials must have effective and timely communications and that the details of disclosures and clinical sponsor relationships should be available to the IRB, particularly as these may pertain to enhancing and clarifying disclosures during consent processes.

OHRP raises the issue of institutional conflicts of interest. We agree that these are serious concerns and merit diligent assessment when such relationships could impinge on the integrity of the research process and the moral responsibilities for involvement of human subjects. However, it seems premature and inappropriate for OHRP to step into this arena in the absence of broader dialogue with the relevant funding agencies, such as NIH. While some institutions already have policies in this area, many do not and it is worrisome that OHRP assigns responsibility to the IRB, which is integral to our institution, in the absence of formal institutional policy and without benchmarks or relevant indicators from clinical research funding agencies.

Finally, we are gravely concerned about the standing this "Guidance" document may take on. The OHRP's FWA document requires compliance (see Term #8 of the posted FWA) with OHRP Guidance. Guidance should not be treated as a matter of regulatory compliance. Institutions and IRBs should have flexibility and discretionary authority to work within the matters covered under "guidance" documents. OHRP should remove the compliance condition with respect to guidance documents.

Overall, while we respect the principled basis for OHRP's initiatives, we conclude that the document is premature in its recommendations and excessively burdensome in its expectations for institutions and IRBs. We urge that the Guidance be set aside until more substantive knowledge of the impact of these recommendations is established. The letter from the Council on Governmental Relations and the Association of American Universities is a thoughtful and comprehensive assessment of the Guidance document. We recommend OHRP give particular attention to their collective recommendations.

Thank you for opportunity to comment on the document.

Sincerely yours,

Mary Ellen Sheridan, Ph.D.  
Associate Vice President for Research